ANIMAL EXPERIMENTATION IN
MEDICINE THROUGH 18th CENTURY

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An Exhibition

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INTRODUCTION

Animal experimentation may be broadly defined as the use of animals for the purpose of increasing knowledge of life processes. This exhibit shows some contributions to medical knowledge through such investigations, from ancient times through the eighteenth century. Not all are monuments in the history of biomedical research: included are several lesser works. Indeed, some are shown as examples of animal experimentation which added little to what we now consider the main lines of development, but which were typical of their period.

During much of the classical period, the dissection of cadavers was prohibited, and animals were used as substitutes in the study of human anatomy. The most important experimental animals were therefore those thought to be most similar to humans in structure, such as the ape, monkey, or the pig. Even these were neglected during the early medieval period, until, with the revival of medical education in Salerno in the 10th century, anatomical demonstrations were again conducted with the pig. Although the occasional dissection of human cadavers gained sanction by the late 13th century, animals continued to serve for centuries as substitutes for the human body as well as for experimental purposes. Thus Blasius, as late as 1673, complained in his tract on the dog of the scarcity of human cadavers and included notes to guide the anatomist on the structural similarities and differences between this animal and man.

As the use of animals declined in the study and teaching of gross human anatomy the emphasis turned during the 17th century to their use in comparative anatomy: Casserio, for example, compared vocal organs of human beings and many types of animals, including birds, mammals, fishes, and reptiles. During the same century the study of developmental anatomy begun by the Greeks was also revived. One of the most important contributions was De Formato Foetu (1604), of Fabricius ab Aquapendente, who examined gravid animals, particularly sheep, and compared the embryos to human fetal development.

Living animals were first used for physiological experiments in antiquity. Erasistratos (d.ca. 304 B.C.) postulated the existence of "emanations" from living creatures, and in what is perhaps the earliest physiological experiment reported, put a bird in a container, starved it, and noted the decrease in weight. Vivisection played an important role in the physiological work of Galen, who used apes, pigs, and dogs. The revival of such investigations in the 16th century is characterized by the work of Vesalius, who repeated many of Galen's experiments on both pig and dog, so that the reader of his De Humani Corporis Fabrica (1543) could compare his technique and findings with those of the Greek master. The 17th century saw the real development of experimental physiology in studies on circulation, respiration, and digestion.

Unlike the more basic biomedical sciences, therapeutics until comparatively recent times has been based almost entirely on experience with humans. Although Paracelsus in the 16th century mentioned the effect of a sulphur compound on a chicken, it was not until the 18th century, that animals were generally used for pharmacological trials. Experimental surgery is another development of the 18th century, although it was suggested much earlier by Vesalius: one should undertake certain dissections, he wrote, "not so much for the sake of knowledge of the organs as in order to train his hands, and to learn to sew up wounds."[1]

While practically the entire range of the animal kingdom has been explored, especially in the fields of comparative anatomy and embryology, certain animals appear repeatedly in the annals of experimental medicine. The dog has been used continuously almost from the beginning of biological investigation for reasons of size, structure, ease of handling, and economy, since it was a common animal with relatively little economic value. The chicken plays a minor but unending role in experimental medicine. One of the earliest identified experimental animals is a chicken in a Hippocratic writing dating from the 6th to 3rd century B.C. A chicken was also the first recorded subject of an experiment in hypnotism made by Kircher in the 17th century.

With the rapid development of physiological experimentation in the 17th century, the smaller animals such as rats, mice, and rabbits figure more prominently in the reports, although the dog continued to be the most commonly used. The "lower animals," such as frogs, lizards, snakes, and salamanders, were also used extensively, for example by Harvey during his experiments on the circulation. The frog in particular became the subject of two important early investigations, Marcello Malpighi's microscopical observations of capillaries in the lung and Jan Swammerdam's muscle-nerve preparations. The guinea pig, which now by extension stands for any subject of experimentation, was introduced into Europe from Peru in the 16th century. Fabricius ab Aquapendente reported on an examination of the guinea pig as early as 1604, but it did not become a common experimental animal until the 18th century.

The conditions of animal experimentation did not materially change from the time of Galen until the introduction of anesthesia and antiseptic surgery in the 19th century. Here is Galen's description of his method of preparation for a vivisection of the spinal cord, (probably in a dog or a pig):

> Provide yourself with a large strong knife ... manufactured from exceptionally good steel .... The animal which you vivisect should not be aged, in order that it may prove easy for you to cut through the vertebrae. For the bones of fully mature animals are, on account of their hardness, difficult to cut .... Lying upon its face, it will be stretched out upon a board, the feet being secured either by means of strong straps, in the manner in which as you know I am accustomed to make them fast, using a board with holes bored in it, or by the hands of assistants.[2]

Scientists, then as now, have been aware that animal experimentation may cause discomfort to the subjects. In a poem by Robert Grove, a contemporary, William Harvey is reported to have expressed the following rationale which, in his mind, and in the minds of many, justified such work:

It is not ferocity of mind, it is not dire lust that makes me cruel, nor is it the mercilessness of a wicked heart; but the sacred hunger for fame, deep within my spirit and in my inmost being, which forces me against my will to make such experiments, and drives away from my breast gentle feelings. It is in my mind to open the dark secrets of nature, to inquire the causes of things once unknown; to release the truth long a captive in chains.[3]

Ellen B. Wells
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1. Andreas Vesalius, De Humani Corporis Fabrica (Basel, 1543), Bk. 7, Ch. 9, S. W. Lambert, trans., in Logan Clendening, Source Book of Medical History (New York, Hoeber, 1942), p. 146.

2. Galen, On Anatomical Procedures: the Later Books (W. L. H. Duckworth, trans., Cambridge, University Press, 1962), p. 20.

3. S. Weir Mitchell, Some Recently Discovered Letters of William Harvey and Other Miscellanea (Philadelphia, College of Physicians, 1912), p. 43.

ANIMAL EXPERIMENTATION IN MEDICINE

Ancient and Medieval

1. Hippocrates. De natura pueri. IN: Hippocrates. De genitura ... interprete Jo. Gorraeo. Paris, 1545.

   Section 29 of this work, part of the Hippocratic corpus but probably by a Cnidian writer, contains one of the earliest suggestions for an animal experiment, an embryological study, in which twenty eggs are set for brooding and one opened each day, providing an opportunity for observation of the developing chick.

   The first separately printed edition appeared in 1542.

2. Rufus of Ephesus, fl. ca. 98-117 A.D. De corporis humani partium appellationibus. IN: Aretaeus. Libri septem. Venice, 1552.

   In his little students' manual for learning anatomical nomenclature, Rufus complains that in earlier days, human dissection was permitted, and that students "learned anatomy fearlessly and with success." He recommends using the monkey as a substitute, "the one which most nearly approaches the man by the arrangement of bones, muscles, viscera, veins and nerves."

   This is the first printed Latin edition, translated by G. P. Grassi.

3. Galen of Pergamon, ca. 129-199 A.D. Opera. Venice, 1490.

   One of the foremost experimental physiologists of all time, Galen's contributions were based on innumerable vivisections and dissections of apes and pigs, with some use of dogs and cattle. Perhaps his best known work concerns the nervous system, for which he generally used pigs or goats.

   This is the first printed collection of Galen's works.

4. Anatomia porci. IN: Mesuë. Mesue vita. [Leyden], 1523.

Compiled for teaching purposes at the School of Salerno some time before 1150, it is often attributed, without basis, to one Copho, a teacher there. For the purposes of internal anatomy (human dissection still being forbidden), the pig was used, as "there are none so like us internally as the pig."

16th century

5. Belon, Pierre, 1517?-1564. L'histoire de la nature des oyseaux, avec leurs descriptions. Paris, 1555.

The revival of comparative anatomy began with the work of Belon, who dissected some two hundred diverse species of birds, and attempted to indicate homologous bone structures in man and bird.

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6. Coiter, Volcher, 1534-1576. Externarum et internarum principalium humani corporis partium tabulae, atque anatomicae exercitationes observationesque. Nuremberg, 1573.

A pupil of Gabriele Falloppio, Coiter was an early student of comparative anatomy, restricting himself to skeletal structure. The principal animal to which he compared the human skeleton was the ape, following Galenic practice. Stimulated, perhaps, by several cases of head injuries, he made some experimental trephinations on dogs, birds, and goats.

7. Paracelsus, 1493-1541. Opera Bücher und Schrifften ... durch Joannem Huserum ... in Truck gegeben. Strassburg, 1603.

In his Von den naturlichen Dingen, written about 1525, Paracelsus refers to what may be the earliest recorded trial of a drug on an animal. This was a sulphur product, which "is sweet, and liked by

chickens, in which it causes a quite harmless sleep."

8. Vesalius, Andreas, 1514-1564. De humani corpis fabrica. Basle, [1543].

The dog was chief subject of Vesalius' studies in physiology, not only for the similarity of its internal structure to man, but also for purposes of comparison with some of Galen's results. Vesalius, by the time he was eighteen, had dissected and vivisected many animals and was already becoming a skilled anatomist.

17th century

9. Accademia del Cimento, Florence. Essays of natural experiments ... Englished by Richard Waller, London, 1684.

Although short-lived, the Accademia, founded by Leopold de' Medici, was the scene of many experiments, including animal experiments.

These essays first appeared in Italian in 1666.

10. Aselli, Gaspare, 1581-1626. De lactibus, sive lacteis venis, quarto vasorum mesaraicorum genere, novo invento. Milan, 1627.

Aselli's discovery of the lacteal vessels took place during a vivisection of a dog in July, 1622, which he held originally to show some friends the function of the recurrent laryngeal nerves——an operation originally performed by Galen.

11. Blasius, Gerard, 1626?-1692? Miscellanea anatomica, hominis, brutorumque variorum. Amsterdam, 1673.

In this little manual of anatomy, Blasius discusses the dog extensively as a substitute for the human cadaver.

12. Borelli, Giovanni Alfonso, 1608-1679. De motu animalium. Rome, 1680-1681.

In his monumental investigations of muscular mechanics, Borelli examined body types and movements of animals such as fishes, birds, and quadrupeds, and compared them to human beings in this regard. His approach was based on the laws of statics and dynamics and took a mathematical bias, as might be expected, perhaps, from a pupil of Galileo.

13. Casserio, Giulio, d. 1616. De vocis auditusque organis historia anatomica. Ferrara, [1601].

Casserio examined a tremendous variety of animals in his investigations of hearing and the production of sound. These were made with human anatomy in mind; his work illustrates adult and fetal human dissections, as well as dogs, cats, rats, cattle, and even fish.

14. Courten, William, 1642-1702. Experiments and observations of the effects of several sorts of poisons upon animals, &c. ... Translated from the Latin ms. Roy. Soc. Phil. Trans. 27:485-501, 1712.

This is one of the earlier reports of trials of various botanical poisons on dogs. Courten, a naturalist and botanist, did his work in 1678-1679, while studying at Montpellier.

15. Fabricius, Hieronymus, ab Aquapendente, 1537-1619. Opera omnia anatomica & physiologica. Leipzig, 1687.

The first description of the formation of the chick in the egg since Aristotle's time is in Fabricius' De formatione ovi et pulli, first published in 1621. In his De formato foetu, published in 1604, he examined mammalian fetuses in detail, with particular attention to the sheep, and with some discussion of fish and snakes. His public anatomies (the term anatomy meaning dissection) attracted many viewers, who occasionally wrote home about them. Thus we know that on January 26, 1584, he gave a public

vivisection of a living gravid ewe, to the great interest of those present.

16. Graaf, Reinier de, 1641-1673. Tractatus anatomico-medicus de succi pancreatici natura & usu. Leyden, 1681.

De Graaf made important studies on pancreatic juice and saliva, collecting these fluids from dogs, using fistulas with tubes from the quills of wild ducks. He was able to compare the pancreatic juice of the dog with that of a sailor who had died suddenly and reported that they had identical properties.

This work was first published in 1664.

17. Grew, Nehemiah, 1641-1712. The comparative anatomy of stomachs and guts begun. London, 1681. Reissued with his Musaeum Regalis Societatis. London, 1694.

Although best known, perhaps, as a plant morphologist and microscopist, Grew used man as a common denominator in comparing the same set of organs in a wide range of animals. He emphasized the necessity of understanding the functions of the organs in order to make valid comparisons.

18. Harvey, William, 1578-1657. Exercitatio anatomica de motu cordis et sanguinis in animalibus. Frankfurt, 1628.

In the course of his investigations on the circulation of the blood, Harvey used forty-nine varieties of animals, and these formed the basis for his conclusions.

19. Kircher, Athanasius, 1602-1680. Ars magna lucis et umbrae. Rome, 1646.

A chicken was used in the first recorded experiment in hypnotism, part of a series in one of Kircher's works on perception and color theory. He called the hypnotic state "actinovolismus," or"brilliant imagination."

20. Malpighi, Marcello, 1628-1694. Opera omnia. Leyden, 1687.

Malpighi's observation of capillaries in a frog's lung was the first use of the microscope with significant scientific results, in this case verifying what Harvey had postulated but not seen thirty-two years before.

His letter to Borelli on this subject was first published in 1661, as De pulmonibus. Observationes anatomicae.

21. Nuck, Anton, 1650-1692. Adenographia curiosa et uteri foeminei anatome nova. Leyden, 1691.

There were many theories of mammalian generation, but very few experiments to test them. Anton Nuck, a professor of anatomy at Leyden made one. He opened a female dog three days after copulation, ligated the uterine horn, and observed pregnancy afterwards, above the ligature. He wrongly concluded that the embryo had been derived from the ovary without fertilization.

22. Pecquet, Jean, 1622-1674. Experimenta nova anatomica. IN: Munier, J.A. De venis tam lacteis thoracicis. Geneva, 1654.

While studying at Montpellier in 1647, Pecquet, in the course of dissecting dogs, worked out the transmission route of chyle from the cisterna chyli through the lacteal vessels into the venous system.

This work was first published in 1651.

23. Redi, Francesco, 1626-1698. Esperienze intorno alla generazione degl' insetti. Florence, 1674.

Redi's use of insects in a "control experiment" involved two sets of jars containing meat, one open, t other with gauze over the tops. In time, maggots appeared within the open jars, but on the gauze cove ing the others, proving that worms did not arise

spontaneously in rotting meat.

24. Severino, Marco Aurelio, 1580-1656. Zootomia Democritaea; id est, Anatome generalis totius animantium opificii. Nuremberg, 1645.

In this, the earliest comprehensive treatise on comparative anatomy, Severino tried to trace analogies of construction in corresponding parts of various animals. He included the text of the Anatomia porci (the last time it was printed as a practical work), and also wrote a section on the qualifications of an anatomist, including ambidexterity and ability to use the microscope. The anatomist, he wrote, must not abominate the human body, and must be ready to explore, with his own hands, the secrets of living things.

25. Steno, Nicolaus, Bp., 1638-1686. Observationes anatomicae. Leyden, 1662.

This includes Steno's account of his discovery of the parotid gland while he was studying at the home of Blasius in 1660. He was dissecting the head of a sheep, and found the duct when his dissecting tool slipped through the gland and clinked against the sheep's teeth.

26. Swammerdam, Jan, 1637-1680. Tractatus physico-anatomico-medicus de respiratione usuque pulmonum. Leyden, 1667.

In a very involved and quite modern series of experiments, Swammerdam used dogs to demonstrate the movements involved in breathing. It is a classic in physiology.

27. Walaeus, Johannes, 1604-1649. Deux lettres ... du mouvement du chyle et du sang. IN: Bartholin, C. Institutions anatomiques. Paris, 1647.

Although at first opposed to Harvey's view of the circulation, Walaeus changed his opinion after experimenting on a dog and demonstrating to his own satisfaction the direction of blood flow in veins.

His letter was first published in 1641.

28. Zambeccari, Giuseppe, 1653-1728. Esperienze ... intorno a diverse viscere tagliate a diversi animali viventi. Florence, 1680.

A pupil of Redi and a pioneer in experimental surgery, Zambeccari performed experimental excisions of various internal organs on dogs and an occasional chicken. One dog survived four consecutive operations.

18th century

29. Abernethy, John, 1764-1831. Surgical and physiological essays. London, 1793.

Abernethy appears to have performed some of the earliest nutrition experiments, desiring to introduce his course of anatomical lectures "with a philosophical account of the nature of the matter, which composes an animal body." He fed a rabbit with lettuce he had grown on flannel and distilled water, and observed that the rabbit rapidly declined.

30. Adams, George, d. 1773. Micrographia illustrata. London, 1766.

This served as a kind of laboratory manual for the many naturalists, biologists, and diletantes who were beginning to collect, observe, and experiment, as well as for anatomists and physiologists. Among the apparatus illustrated is a handy rack for stretching frog preparations.

31. Beddoes, Thomas, 1760-1808, and James Watt, 1736-1819. Considerations on the medicinal use and on the production of factitious airs. 2d ed. Bristol, 1795.

In the process of developing what became pneumotherapy, Beddoes used puppies, kittens, and rabbits to test the various airs and atmospheres created in James Watts' newly constructed apparatus.

32. Crawford, Adair, 1748-1795. Experiments and observations on animal heat. 2d ed. London, 1788.

One of the earliest uses of guinea pigs was in the summer of 1777, when Crawford began his careful investigations of animal heat. His method involved water calorimetry.

33. Douglas, Sylvester, 1743-1823. Dissertatio medica inauguralis de stimulis. Leyden, 1766.

This student dissertation is a rambling discourse on stimulation and movement, following the lead of Haller and Whytt. The author performed several experiments, using as subjects six rabbits, two sheep and one dog.

34. Fontana, Felix, 1730-1805. Treatise on the venom of the viper. London, 1787.

Fontana, naturalist to the Grand Duke of Tuscany, used guinea pigs, frogs, and rabbits. He tested the effects of viper venom on various bodily fluids and tissues, for example blood, tendons, and nerves, and often used controls.

This work was first published in 1767.

35. Galvani, Luigi, 1737-1798. De viribus electricitatis in motu musculari. Modena, 1792.

The frog was the chief subject in Galvani's studies of electrical phenomena in organisms.

36. Hales, Stephen, 1677-1761. Statical essays: containing haemastaticks. Vol. II. London, 1733.

An English clergyman, and an amateur in science, Hales made important contributions to the understanding of the mechanics of blood pressure. Using several horses, he measured the bood pressure by means of tubes inserted in an artery. He also used dogs and other animals. The horses, Hales tells us, were all unfit for service and would in any case have been destroyed.

37. Haller, Albrecht von, 1708-1777. A dissertation on the sensible and irritable parts of animals. Translated from the Latin ... by M. Tissot. London, 1755.

The multitudinous contributions of Haller, one of the greatest physiologists of all time, include a series of experiments made in Göttingen in the early 1750's, in which he distinguished between nerve impulse and muscle contraction. For these experiments, he used dogs and goats, as well as rats, cats, and rabbits.

Haller, like Harvey, felt sympathy for his subjects:

> ... and since the beginning of the year 1751 I have examined several different ways, a hundred and ninety animals, a species of cruelty for which I felt such a reluctance, as could only be overcome by the desire of contributing to the benefit of mankind, and excused by that motive which induces persons of the most humane temper, to eat every day the flesh of harmless animals without scruple.

His memoir on these experiments was originally read in the Academy at Göttingen in April, 1752.

38. Home, Evrard, 1756-1832. An account of Mr. Hunter's method of performing the operation for the cure of the poplitean aneurism. Soc. for the Improvement of Med. and Chir. Knowledge. Trans. 1:138-181, 1793.

Based on his experiments with Richmond Park deer and with dogs, John Hunter (1728-1793) developed an improved method of tying off aneurysms.

39. Kite, Charles, d. 1811. Essays and observations, physiological and medical, on the submersion of animals. London, 1795.

In 1788, Kite, a medical writer and practitioner at Gravesend, won the silver medal from the Humane Societ for his work on recovery of the apparently dead. He

continued his investigations on various aspects of drowning, using cats and dogs.

40. Leigh, John, fl. 1785. An experimental inquiry into the properties of opium, and its effects on living subjects. Edinburgh, 1786.

While in Edinburgh, John Leigh of Virginia produced this careful, critical study of opium, testing its qualities on dogs and rabbits. It did not really add anything new, but was typical of the dawning style of experimental inquiry.

His work is dedicated to George Washington, "a man equally revered by the friends and foes of his country."

41. Monro, Alexander, 1733-1817. Experiments on the nervous system, with opium and metalline substances. Edinburgh, 1793.

On the basis of his experiments with the effect of opium on the tissues of frogs, Monro concluded that nerve force was not equal to electrical force. By this time, the frog had become a relatively common experimental animal.

42. Murray, Andreas Johann Georg, 1740-1791. Commentatio de redintegratione partium corporis animalis nexu suo solutarum vel amissarum. Göttingen, 1787.

The restoration of injured tissue was the subject of a debate which took place before the medical faculty of Göttingen in June of 1787. Murray, a naturalist, contended that most tissue could not be made to restore itself and gave as proof copius literature citations and records of his experiments on 17 dogs, 4 rabbits, and 1 chicken. He was able, in one case, to replace part of a tendon with a ligament.

43. Priestley, Joseph, 1733-1804. Experiments and observations on different kinds of air. 2d ed. corr. London, 1775.

Priestley used rats and mice when proving the necessity of oxygen to the maintenance of life. He included in his introduction to the work shown some comments on the capture and care of his laboratory subjects.

44. Smith, Thomas, fl. 1805. An essay on wounds of the intestines [an inaugural essay ... University of Pennsylvania] Philadelphia, 1805.

In a rather unusual thesis, Smith, a student from the island of St. Croix, tried various stitching techniques on dogs, in an attempt to improve intestinal wound repair. Of the eleven dogs used, six survived and were later sacrificed for evaluations of the repair.

45. Spallanzani, Lazzaro, 1729-1799. An essay on animal reproductions ... Translated [by M. Mary] London, 1769.

Confining himself to snails, salamanders, frogs, and worms, Spallanzani conducted a series of experiments on tissue regeneration and recorded microscopic observations of the reforming tissue. A man of great experimental skill, he also did important work on digestion and generation.

This work was originally published in Modena in 1768, as Prodromo di un opera da imprimersi sopra le riproduzioni animali.

46. Stevens, Edward W., fl. 1777. Dissertatio physiologica inauguralis, de alimentorum concoctione. Edinburgh, 1777.

In his digestion experiments, Stevens used small perforated silver spheres, in which various types of food were placed. These were swallowed by dogs, sheep, and cattle, and by one man "of weak understanding who swallowed stones for the amusement of the common people." Stevens concluded, as did Spallanzani at about the same time, that digestion was not accomplished by heat, putrefaction, or fermentation, but by a "solvent" secreted by the stomach.

47. Sue, Jean-Joseph, 1760-1830. Recherches physiologiques, et expériences sur la vitalité. Paris, An VI (1797).

Opposed to the use of the guillotine on the grounds that the parts severed might continue to live for some time and have sensations, Sue conducted trial decollations on chickens, frogs, rabbits, and cattle to prove his point. He also stated clearly that animal experimentation had valid meaning for human life.

48. Townson, Robert, fl. 1792-1799. Tracts and observations in natural history and physiology. London, 1799.

The studies on amphibian anatomy and physiology in this work were originally made by Townson in Göttingen for his medical degree, granted in 1795. It may have had some value as a laboratory aid.

49. Trembley, Abraham, 1710-1784. Mémoires, pour servir à l'histoire d' un genre de polypes d'eau douce. Leyden, 1744.

The first view of cell division was seen in a hydra, by Trembley, using a hand lens. He was also the first to make permanent grafts of animal tissue, again using the hydra (discovered some 39 years before by Leeuwenhoek), and thus laying the groundwork for experimental morphology.

50. [Whytt, Robert] 1714-1766. An essay on the vital and other involuntary motions of animals. 2d ed., with corr. and add. Edinburgh, 1763.

Probably the foremost neurologist of his time, Whytt, on the basis of his experiments on decapitated frogs, birds, some eels, and a snake, suggested that the soul was equally distributed throughout the nervous system. He investigated reflex action as well.

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